

60020830-0003.ST25
SEQUENCE LISTING

<110> Wun, Tze-Chein
Wun, Tze-Chein

<120> Novel Recombinant Anticoagulant Proteins

<130> 60020830-0003

<160> 41

<170> PatentIn version 3.1

<210> 1
<211> 382
<212> PRT
<213> Artificial

<220>
<223> Fusion protein: human-derived ANV with TAP

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20 25 30

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35 40 45

Tyr Tyr Ser Ser Tyr Asn Asp Cys Phe Asn Ala Cys Ile Gly Ser Ala
50 55 60

Gln Val Leu Arg Gly Thr Val Thr Asp Phe Pro Gly Phe Asp Glu Arg
65 70 75 80

Ala Asp Ala Glu Thr Leu Arg Lys Ala Met Lys Gly Leu Gly Thr Asp
85 90 95

Glu Glu Ser Ile Leu Thr Leu Leu Thr Ser Arg Ser Asn Ala Gln Arg
100 105 110

Gln Glu Ile Ser Ala Ala Phe Lys Thr Leu Phe Gly Arg Asp Leu Leu
115 120 125

Asp Asp Leu Lys Ser Glu Leu Thr Gly Lys Phe Glu Lys Leu Ile Val
130 135 140

Ala Leu Met Lys Pro Ser Arg Leu Tyr Asp Ala Tyr Glu Leu Lys His
145 150 155 160

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Ala Leu Lys Gly Ala Gly Thr Asn Glu Lys Val Leu Thr Glu Ile Ile
165 170 175

Ala Ser Arg Thr Pro Glu Glu Leu Arg Ala Ile Lys Gln Val Tyr Glu
180 185 190

Glu Glu Tyr Gly Ser Ser Leu Glu Asp Asp Val Val Gly Asp Thr Ser
195 200 205

Gly Tyr Tyr Gln Arg Met Leu Val Val Leu Leu Gln Ala Asn Arg Asp
210 215 220

Pro Asp Ala Gly Ile Asp Glu Ala Gln Val Glu Gln Asp Ala Gln Ala
225 230 235 240

Leu Phe Gln Ala Gly Glu Leu Lys Trp Gly Thr Asp Glu Glu Lys Phe
245 250 255

Ile Thr Ile Phe Gly Thr Arg Ser Val Ser His Leu Arg Lys Val Phe
260 265 270

Asp Lys Tyr Met Thr Ile Ser Gly Phe Gln Ile Glu Glu Thr Ile Asp
275 280 285

Arg Glu Thr Ser Gly Asn Leu Glu Gln Leu Leu Leu Ala Val Val Lys
290 295 300

Ser Ile Arg Ser Ile Pro Ala Tyr Leu Ala Glu Thr Leu Tyr Tyr Ala
305 310 315 320

Met Lys Gly Ala Gly Thr Asp Asp His Thr Leu Ile Arg Val Met Val
325 330 335

Ser Arg Ser Glu Ile Asp Leu Phe Asn Ile Arg Lys Glu Phe Arg Lys
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370 375 380

<210> 2
<211> 378
<212> PRT
<213> Artificial

<220>
<223> Fusion protein: human-derived ANV with artificial 6L15 (a variant
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of naturally occurring bovine pancreatic trypsin inhibitor)

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35 40 45

Arg Gln Glu Ile Ser Ala Ala Phe Lys Thr Leu Phe Gly Arg Asp Leu
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Leu Asp Asp Leu Lys Ser Glu Leu Thr Gly Lys Phe Glu Lys Leu Ile
65 70 75 80

Val Ala Leu Met Lys Pro Ser Arg Leu Tyr Asp Ala Tyr Glu Leu Lys
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His Ala Leu Lys Gly Ala Gly Thr Asn Glu Lys Val Leu Thr Glu Ile
100 105 110

Ile Ala Ser Arg Thr Pro Glu Glu Leu Arg Ala Ile Lys Gln Val Tyr
115 120 125

Glu Glu Glu Tyr Gly Ser Ser Leu Glu Asp Asp Val Val Gly Asp Thr
130 135 140

Ser Gly Tyr Tyr Gln Arg Met Leu Val Val Leu Leu Gln Ala Asn Arg
145 150 155 160

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165 170 175

Ala Leu Phe Gln Ala Gly Glu Leu Lys Trp Gly Thr Asp Glu Glu Lys
180 185 190

Phe Ile Thr Ile Phe Gly Thr Arg Ser Val Ser His Leu Arg Lys Val
195 200 205

Phe Asp Lys Tyr Met Thr Ile Ser Gly Phe Gln Ile Glu Glu Thr Ile
210 215 220

Asp Arg Glu Thr Ser Gly Asn Leu Glu Gln Leu Leu Leu Ala Val Val
225 230 235 240

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Lys Ser Ile Arg Ser Ile Pro Ala Tyr Leu Ala Glu Thr Leu Tyr Tyr
 245 250 255

Ala Met Lys Gly Ala Gly Thr Asp Asp His Thr Leu Ile Arg Val Met
 260 265 270

Val Ser Arg Ser Glu Ile Asp Leu Phe Asn Ile Arg Lys Glu Phe Arg
 275 280 285

Lys Asn Phe Ala Thr Ser Leu Tyr Ser Met Ile Lys Gly Asp Thr Ser
 290 295 300

Gly Asp Tyr Lys Lys Ala Leu Leu Leu Leu Ala Gly Glu Asp Asp Met
 305 310 315 320

His Pro Asp Phe Cys Leu Glu Pro Pro Tyr Asp Gly Pro Cys Arg Ala
 325 330 335

Leu His Leu Arg Tyr Phe Tyr Asn Ala Lys Ala Gly Leu Cys Gln Thr
 340 345 350

Phe Tyr Tyr Gly Gly Cys Leu Ala Lys Arg Asn Asn Phe Glu Ser Ala
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Glu Asp Cys Met Arg Thr Cys Gly Gly Ala
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<210> 3
 <211> 376
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 <213> Artificial

<220>
 <223> Fusion protein: human-derived ANV with synthetic human K-APP

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 35 40 45

Arg Gln Glu Ile Ser Ala Ala Phe Lys Thr Leu Phe Gly Arg Asp Leu
 50 55 60

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Leu Asp Asp Leu Lys Ser Glu Leu Thr Gly Lys Phe Glu Lys Leu Ile
 65 70 75 80

Val Ala Leu Met Lys Pro Ser Arg Leu Tyr Asp Ala Tyr Glu Leu Lys
 85 90 95

His Ala Leu Lys Gly Ala Gly Thr Asn Glu Lys Val Leu Thr Glu Ile
 100 105 110

Ile Ala Ser Arg Thr Pro Glu Glu Leu Arg Ala Ile Lys Gln Val Tyr
 115 120 125

Glu Glu Glu Tyr Gly Ser Ser Leu Glu Asp Asp Val Val Gly Asp Thr
 130 135 140

Ser Gly Tyr Tyr Gln Arg Met Leu Val Val Leu Leu Gln Ala Asn Arg
 145 150 155 160

Asp Pro Asp Ala Gly Ile Asp Glu Ala Gln Val Glu Gln Asp Ala Gln
 165 170 175

Ala Leu Phe Gln Ala Gly Glu Leu Lys Trp Gly Thr Asp Glu Glu Lys
 180 185 190

Phe Ile Thr Ile Phe Gly Thr Arg Ser Val Ser His Leu Arg Lys Val
 195 200 205

Phe Asp Lys Tyr Met Thr Ile Ser Gly Phe Gln Ile Glu Glu Thr Ile
 210 215 220

Asp Arg Glu Thr Ser Gly Asn Leu Glu Gln Leu Leu Leu Ala Val Val
 225 230 235 240

Lys Ser Ile Arg Ser Ile Pro Ala Tyr Leu Ala Glu Thr Leu Tyr Tyr
 245 250 255

Ala Met Lys Gly Ala Gly Thr Asp Asp His Thr Leu Ile Arg Val Met
 260 265 270

Val Ser Arg Ser Glu Ile Asp Leu Phe Asn Ile Arg Lys Glu Phe Arg
 275 280 285

Lys Asn Phe Ala Thr Ser Leu Tyr Ser Met Ile Lys Gly Asp Thr Ser
 290 295 300

Gly Asp Tyr Lys Lys Ala Leu Leu Leu Leu Ala Gly Glu Asp Asp Glu
 305 310 315 320

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Val Cys Ser Glu Gln Ala Glu Thr Gly Pro Cys Arg Ala Met Ile Ser
 325 330 335

Arg Trp Tyr Phe Asp Val Thr Glu Gly Lys Cys Ala Pro Phe Phe Tyr
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Met Ala Val Cys Gly Ser Ala Ile
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<211> 459

<212> PRT

<213> Artificial

<220>

<223> Fusion protein: human-derived ANV with KK-TFPI (a human sequence)

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 20 25 30

Asp Glu Glu Ser Ile Leu Thr Leu Leu Thr Ser Arg Ser Asn Ala Gln
 35 40 45

Arg Gln Glu Ile Ser Ala Ala Phe Lys Thr Leu Phe Gly Arg Asp Leu
 50 55 60

Leu Asp Asp Leu Lys Ser Glu Leu Thr Gly Lys Phe Glu Lys Leu Ile
 65 70 75 80

Val Ala Leu Met Lys Pro Ser Arg Leu Tyr Asp Ala Tyr Glu Leu Lys
 85 90 95

His Ala Leu Lys Gly Ala Gly Thr Asn Glu Lys Val Leu Thr Glu Ile
 100 105 110

Ile Ala Ser Arg Thr Pro Glu Glu Leu Arg Ala Ile Lys Gln Val Tyr
 115 120 125

Glu Glu Glu Tyr Gly Ser Ser Leu Glu Asp Asp Val Val Gly Asp Thr
 130 135 140

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Ser Gly Tyr Tyr Gln Arg Met Leu Val Val Leu Leu Gln Ala Asn Arg
 145 150 155 160

Asp Pro Asp Ala Gly Ile Asp Glu Ala Gln Val Glu Gln Asp Ala Gln
 165 170 175

Ala Leu Phe Gln Ala Gly Glu Leu Lys Trp Gly Thr Asp Glu Glu Lys
 180 185 190

Phe Ile Thr Ile Phe Gly Thr Arg Ser Val Ser His Leu Arg Lys Val
 195 200 205

Phe Asp Lys Tyr Met Thr Ile Ser Gly Phe Gln Ile Glu Glu Thr Ile
 210 215 220

Asp Arg Glu Thr Ser Gly Asn Leu Glu Gln Leu Leu Leu Ala Val Val
 225 230 235 240

Lys Ser Ile Arg Ser Ile Pro Ala Tyr Leu Ala Glu Thr Leu Tyr Tyr
 245 250 255

Ala Met Lys Gly Ala Gly Thr Asp Asp His Thr Leu Ile Arg Val Met
 260 265 270

Val Ser Arg Ser Glu Ile Asp Leu Phe Asn Ile Arg Lys Glu Phe Arg
 275 280 285

Lys Asn Phe Ala Thr Ser Leu Tyr Ser Met Ile Lys Gly Asp Thr Ser
 290 295 300

Gly Asp Tyr Lys Lys Ala Leu Leu Leu Leu Ala Gly Glu Asp Asp Met
 305 310 315 320

His Ser Phe Cys Ala Phe Lys Ala Asp Asp Gly Pro Cys Lys Ala Ile
 325 330 335

Met Lys Arg Phe Phe Phe Asn Ile Phe Thr Arg Gln Cys Glu Glu Phe
 340 345 350

Ile Tyr Gly Gly Cys Glu Gly Asn Gln Asn Arg Phe Glu Ser Leu Glu
 355 360 365

Glu Cys Lys Lys Met Cys Thr Arg Asp Asn Ala Asn Arg Ile Ile Lys
 370 375 380

Thr Thr Leu Gln Gln Glu Lys Pro Asp Phe Cys Phe Leu Glu Glu Asp
 385 390 395 400

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Pro Gly Ile Cys Arg Gly Tyr Ile Thr Arg Tyr Phe Tyr Asn Asn Gln
 405 410 415

Thr Lys Gln Cys Glu Arg Phe Lys Tyr Gly Gly Cys Leu Gly Asn Met
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Asn Asn Phe Glu Thr Leu Glu Glu Cys Lys Asn Ile Cys Glu Asp Gly
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Pro Asn Gly Phe Gln Val Asp Asn Tyr Gly Thr
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 <213> Artificial

<220>
 <223> Fusion gene of human-derived ANV with TAP

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<210> 6
<211> 1137
<212> DNA
<213> Artificial

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<220>
<223> Fusion gene of human-derived ANV with artificial 6L15, which is a
variant of naturally occurring bovine pancreatic trypsin inhibit
or

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<213> Artificial

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<223> Fusion gene of human-derived ANV with synthetic human K-APP gene

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<211> 1380

<212> DNA

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<223> Fusion gene of human-derived ANV with KK-TFPI, which is a human sequence

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ttgacatccc gaagtaatgc tcagcgccag gaaatctctg cagcttttaa gactctgttt    180
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 <212> DNA
 <213> Homo sapiens

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 <212> PRT
 <213> Homo sapiens

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 35 40 45

Arg Gln Glu Ile Ser Ala Ala Phe Lys Thr Leu Phe Gly Arg Asp Leu
 50 55 60

Leu Asp Asp Leu Lys Ser Glu Leu Thr Gly Lys Phe Glu Lys Leu Ile
 65 70 75 80

Val Ala Leu Met Lys Pro Ser Arg Leu Tyr Asp Ala Tyr Glu Leu Lys
 85 90 95

His Ala Leu Lys Gly Ala Gly Thr Asn Glu Lys Val Leu Thr Glu Ile
 100 105 110

Ile Ala Ser Arg Thr Pro Glu Glu Leu Arg Ala Ile Lys Gln Val Tyr
 115 120 125

Glu Glu Glu Tyr Gly Ser Ser Leu Glu Asp Asp Val Val Gly Asp Thr
 130 135 140

Ser Gly Tyr Tyr Gln Arg Met Leu Val Val Leu Leu Gln Ala Asn Arg
 145 150 155 160

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Asp Pro Asp Ala Gly Ile Asp Glu Ala Gln Val Glu Gln Asp Ala Gln
 165 170 175

Ala Leu Phe Gln Ala Gly Glu Leu Lys Trp Gly Thr Asp Glu Glu Lys
 180 185 190

Phe Ile Thr Ile Phe Gly Thr Arg Ser Val Ser His Leu Arg Lys Val
 195 200 205

Phe Asp Lys Tyr Met Thr Ile Ser Gly Phe Gln Ile Glu Glu Thr Ile
 210 215 220

Asp Arg Glu Thr Ser Gly Asn Leu Glu Gln Leu Leu Leu Ala Val Val
 225 230 235 240

Lys Ser Ile Arg Ser Ile Pro Ala Tyr Leu Ala Glu Thr Leu Tyr Tyr
 245 250 255

Ala Met Lys Gly Ala Gly Thr Asp Asp His Thr Leu Ile Arg Val Met
 260 265 270

Val Ser Arg Ser Glu Ile Asp Leu Phe Asn Ile Arg Lys Glu Phe Arg
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33

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31

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<210> 13
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 <212> DNA
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<220>
 <223> Synthetic oligonucleotide used to generate ANV cDNA mutation of Cys-to-Ala at position 315

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<210> 14
 <211> 960
 <212> DNA
 <213> Artificial

<220>
 <223> Sequence encoding human ANV with Cys-to-Ala mutation at position 315

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 ttgacatccc gaagtaatgc tcagcgccag gaaatctctg cagcttttaa gactctgttt 180
 ggcagggatc ttctggatga cctgaaatca gaactaactg gaaaatttga aaaattaatt 240
 gtggctctga tgaaacctc tcggctttat gatgcttatg aactgaaaca tgccttgaag 300
 ggagctggaa caaatgaaaa agtactgaca gaaattattg cttcaaggac acctgaagaa 360
 ctgagagcca tcaacaagt ttatgaagaa gaatatggct caagcctgga agatgacgtg 420
 gtgggggaca cttcagggtg ctaccagcgg atgttggtgg ttctccttca ggctaacaga 480
 gaccctgatg ctggaattga tgaagctcaa gttgaacaag atgctcaggc tttatttcag 540
 gctggagaac ttaaatggg gacagatgaa gaaaagttta tcaccatctt tggaacacga 600
 agtgtgtctc atttgagaaa ggtgtttgac aagtacatga ctatatcagg atttcaaatt 660
 gaggaacca ttgaccgca gacttctggc aatttagagc aactactcct tgctgttgtg 720
 aaatctattc gaagtatacc tgccctacct gcagagacct tctattatgc tatgaaggga 780
 gctgggacag atgatcatc cctcatcaga gtcattggtt ccaggagtga gattgatctg 840
 tttaacatca ggaaggagtt taggaagaat ttgcccact ctctttattc catgattaag 900
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<210> 15
 <211> 64
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 <213> Artificial

<220>

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<223> Synthetic oligonucleotide, first of three forward primers used to generate recombinant 6L15 gene

<400> 15
 tccggacttc tgcttgaac cgccgtacga cgggtccgtgc cgtgctctgc acctgcgtta 60
 cttc 64

<210> 16
 <211> 60
 <212> DNA
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<220>
 <223> Synthetic oligonucleotide, second of three forward primers used to generate recombinant 6L15

<400> 16
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<210> 17
 <211> 50
 <212> DNA
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<220>
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<400> 17
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<210> 18
 <211> 63
 <212> DNA
 <213> Artificial

<220>
 <223> Synthetic oligonucleotide, first of three reverse primers used to generate recombinant 6L15 gene

<400> 18
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<210> 19
 <211> 60
 <212> DNA
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<220>
 <223> Synthetic oligonucleotide, second of three reverse primers used to generate recombinant 6L15 gene

<400> 19
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<210> 20
 <211> 60
 <212> DNA
 <213> Artificial

<220>
 <223> Synthetic oligonucleotide, third of three reverse primers used to generate recombinant 6L15 gene

<400> 20
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<210> 21
 <211> 177
 <212> DNA
 <213> Artificial

<220>
 <223> synthetic 6L15 gene

<400> 21
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 tactttctaca atgcaaaggc aggcctgtgt cagaccttct actacggcgg ttgcctggct 120
 aagcgtaaca acttcgaatc cgcggaagac tgcattgcgta cttgcggtgg tgcttaa 177

<210> 22
 <211> 186
 <212> DNA
 <213> Artificial

<220>
 <223> Synthetic, derived from Ornithodoros moubata gene

<400> 22
 gcttacaacc gtctgtgcat caaaccgcgt gactggatcg acgaatgcga ctccaacgaa 60
 ggtggtgaac gtgcttactt ccgtaacggt aaaggtgggt gcgactcctt ctggatctgc 120
 ccggaagacc acaccggtgc tgactactac tcctcctacc gtgactgctt caacgcttgc 180
 atctaa 186

<210> 23
 <211> 122
 <212> DNA
 <213> Artificial

<220>
 <223> forward synthetic oligonucleotide for generating synthetic K-APP gene with flanking sequences

<400> 23
 ggccctaccc cacagatacg gagttgccac cactgaaact tgaggttggt agagagggtt 60
 gttctgagca agctgagact ggtccatgta gagctatgat ttctagatgg tacttcgacg 120
 tt 122

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<210> 24
 <211> 117
 <212> DNA
 <213> Artificial

<220>
 <223> forward synthetic oligonucleotide for generating synthetic K-APP gene with flanking sequences

<400> 24
 actgagggta agtgtgctcc attcttctac ggtggttggtg gtggtaacag aaacaacttc 60
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<210> 25
 <211> 124
 <212> DNA
 <213> Artificial

<220>
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<400> 25
 ctcaagtaacg tcgaagtacc atctagaaat catagctcta catggaccag tctcagcttg 60
 ctcaagaaca acctctctaa caacctcaag tttcagtggt ggcaactccg tatctgtggg 120
 gtag 124

<210> 26
 <211> 115
 <212> DNA
 <213> Artificial

<220>
 <223> reverse synthetic oligonucleotide for generating synthetic K-APP gene with flanking sequences

<400> 26
 agcttcatca atgcatttaa atagcagaac cacaacacgc catacagtac tcctcagtggt 60
 cgaagttggt tctgtttacca ccacaaccac cgtagaagaa tggagcacac ttacc 115

<210> 27
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 <212> DNA
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<220>
 <223> synthetic K-APP gene, derived from human sequence

<400> 27
 gagggtttgtt ctgagcaagc tgagactggt ccatgtagag ctatgatttc tagatggtac 60
 ttcgacgtta ctgagggtaa gtgtgctcca ttcttctacg gtggttggtg tggtaacaga 120
 aacaacttcg aactgagga gtactgtatg gctgtttgtg gttctgctat ttaa 174

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<210> 28
<211> 30
<212> DNA
<213> Artificial

<220>
<223> primer

<400> 28
ggaattccat atggcacagg ttctcagagg

30

<210> 29
<211> 24
<212> DNA
<213> Artificial

<220>
<223> primer

<400> 29
ccaatgcatg tcattttctc cagc

24

<210> 30
<211> 24
<212> DNA
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<220>
<223> primer

<400> 30
ccaatgcatc cggacttctg cctg

24

<210> 31
<211> 24
<212> DNA
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<220>
<223> primer

<400> 31
ccaatgcatt cattttgtgc attc

24

<210> 32
<211> 27
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<220>
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<400> 32
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27

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<212> DNA
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<220>
 <223> primer

<400> 33
 acgcgtcgac ttaggtcca taattatcc 29

<210> 34
 <211> 30
 <212> DNA
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<220>
 <223> primer

<400> 34
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<210> 35
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 <212> DNA
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<220>
 <223> primer

<400> 35
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<210> 36
 <211> 26
 <212> DNA
 <213> Artificial

<220>
 <223> primer

<400> 36
 cgggatccgc acaggttctc agaggc 26

<210> 37
 <211> 29
 <212> DNA
 <213> Artificial

<220>
 <223> primer

<400> 37
 acgcgtcgac ttagtcatct tctccagcg 29

<210> 38
 <211> 31
 <212> DNA
 <213> Artificial

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<220>
<223> primer designed for generating PCR fragment of interest for cloning into vector pPIC9

<400> 38
ccgctcgaga aaagagcaca ggttctcaga g 31

<210> 39
<211> 33
<212> DNA
<213> Artificial

<220>
<223> primer designed for generating PCR fragment of interest for cloning into yeast expression vector pPIC9

<400> 39
ataagaatgc ggccgcttaa atagcagaac cac 33

<210> 40
<211> 24
<212> DNA
<213> Artificial

<220>
<223> primer designed for generating PCR fragment of interest for cloning into yeast expression vector pPIC9

<400> 40
cgcgatatca tcttctccag cgag 24

<210> 41
<211> 20
<212> DNA
<213> Artificial

<220>
<223> primer designed for generating PCR fragments of interest for cloning into yeast expression vector pPIC9

<400> 41
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